REMARKS

This amendment is being filed in response to the Official Action mailed in this application on January 17, 2001. A request for extension of time (three months) accompanies this amendment. Also accompanying this amendment are a cover sheet for paying additional fees, and a supplemental information disclosure statement. Reconsideration of this application is respectfully requested in view of the above amendments and further in view of the following remarks.

First, applicant appreciates the Examiner's review of the art already cited by applicant. However, applicant notes that WO99/03476 was relied upon in application serial no. 09/432,465, but was not cited by the Examiner in this application. For completeness, applicant is submitting herewith a supplemental information disclosure statement including this document. Also included in the supplemental information disclosure statement is Hermann et al and U.S. 6,153,632. Hermann et al is listed in the references of Erle et al. (Erle et al was cited by the Examiner in this application); and U.S. 6,153,632 has come to the attention of applicant.

Turning to the action on the merits, applicant notes that claims 1-36 were rejected under 35 U.S.C. §112, second paragraph. Applicant has rewritten claims 1-36 as new claims 37-72, respectively. Reconsideration of this rejection is respectfully requested.

First, claims 1 and 22-25 were rejected for the reason that the expressions "first line treatment" and "drug naïve human patient" are not clear. Claims 1 and 22-25 correspond to new claims 37 and 58-61. Applicant has not amended these expressions since it is believed that they are clear and known to those in the art. Moreover, the expressions are used throughout the specification and certainly are clear in that context. For example, "first line treatment" refers to initial therapy (see, *e.g.*, page 13, line 12; page 27, lines 2-14; page 29, lines 16-24; and page 34, lines 30-37) and "drug naïve human patient" refers to a human patient who has had no drug therapy (see, *e.g.*, page 25, lines 8-10 and line 36-37; page 26, lines 6-7; and page 29, lines 16-24).

Claims 3 and 21 were rejected for use of the term "substantially" in the expression "substantially equivalent efficacy". Again, applicant has not amended claims 3 and 21, now claims 39 and 57. The expression "at least substantially equivalent efficacy" is specifically defined in the specification on page 16, line 23-33.

Next, the rejection indicates that claims 3 and 32-34 fail to further limit claim 1. Claim 1 is now claim 37, and claims 3 and 32-34 are now claims 39 and 68-70. Claim 37 defines a method for first line treatment of type 2 diabetes in a drug naïve human patient. Claim 39 further refines the method to require substantially reduced side effects, and claims 68-70 specify and refine the side effects. Applicant believes these claims are properly presented as written.

Claims 4-7 were rejected since claim 1 was said not to provide antecedent basis for the expressions "starting daily dosage" and "daily maintenance dosage". Claims 4-7 were amended and rewritten as claims 40-43. Applicant believes that the amendment obviates this portion of the rejection.

Claims 5 and 19, and claims 7 and 20 were rejected for failing to further limit the claims from which they depend. However, the combination in all the claims includes metformin and glyburide. It is clear from the specification that "low dose" can refer to the dose of metformin, the dose of glyburide or the dose of both. Claims 5 and 19 (now claims 41 and 55) encompass the situation where the dose of glyburide is always a "low dose", and the dose of metformin can be a low dose or up to the dose normally employed. Similarly, claims 7 and 20 (now claims 43 and 56) encompass the situation where the dose of metformin is always a low dose, and the dose of glyburide can be a low dose or up to the dose normally employed.

Claims 14-16 (now claims 50-52) were rejected for use of the word "contains". The claims were changed to read - -comprises- - as suggested by the Examiner.

Claims 17-18 (now claims 53-54) were rejected since claim 1 was said not to provide antecedent basis for the expression "metformin/glyburide dosage". Original claims 14-18 have been rewritten as new claims 50-54. In claims 50-53, "metformin/glyburide" has been amended to read - - the combination of metformin and glyburide - -, and in claim 54, "metformin/glyburide 250 mg/1.25 mg dosage" has been amended to read - - the 250 mg metformin/1.25 mg glyburide dosage - -. Applicant believes there is clear antecedent basis for all these expressions.

Claim 18 (now claim 54) was rejected for use of the term "HbA_{1c}". According to the rejection, the term should be fully identified the first time it is used. Although this term is well know, claim 54 was amended as requested by the Examiner. Support for the amendment can be found in the specification at, for example, page 12, line 9.

Next, claims 18-20 (now claims 54-56) were rejected for use of the expressions "where necessary" and "generally accepted medical practice". Applicant believes these expressions are clear as written but would be happy to entertain any suggested amendments made by the Examiner.

Claim 21 was rejected for its use of the expression "characterized in that". The Examiner suggested amending the expression to read - - wherein - -. However, the term "wherein" already appeared in the claim. Consequently, claim 21 was rewritten as claim 57 so that, applicant believes, the rejection has been obviated.

Claims 27 and 28 were rejected for the use of the term "such", and the Examiner indicated that amending the term to read - - so - - would overcome the rejection. Claims 27 and 28 have been rewritten as new claims 63 and 64 as suggested by the Examiner.

Claim 25 was rejected for the use of the expression "wherein the glyburide is such that the glyburide bioavailability is comparable to the glyburide bioavailability obtained with a separate administration of metformin and glyburide". Applicant believes this expression is clear as written but again would be happy to entertain any suggested amendments made by the Examiner.

Applicant appreciates the error noted by the Examiner in claim 29 (now claim 65). This error has been corrected in the rewritten claim.

Claim 30 (now claim 66) has been rejected for use of the expression "undersize value". Applicant submits that this expression is well known to those in the art. For example, claim 66 reads in part: the glyburide has a particle size distribution of about 25% undersize value not more than 6 μm. Those in the art would understand that this means that 25% of the particles, by weight, are smaller than 6 μm.

Applicant appreciates the error noted in claims 35 and 36 regarding the expression "pharmaceutical formulation as defined in claim 1" when claim 1 was a method claim. Claims 35 and 36 have been rewritten as new independent claims 71 and 72. Accordingly, applicant believes this rejection has been obviated.

Finally, claim 36 was rejected for use of the term "and/or". When claim 36 was rewritten as new claim 72, the term "and/or" was removed. Accordingly, applicant believes this rejection has been obviated.

For all these reasons, applicant believes that claims 1-36 comply with the requirements of 35 U.S.C. §112, second paragraph. Therefore, it is respectfully requested that the rejection under 35 U.S.C. §112 be withdrawn.

Claims 1-36 were also rejected under 35 U.S.C. §103(a) as being unpatentable over Press Release 09/30/99: Bristol-Myers Squibb Files New Drug Application for Novel Oral Antidiabetic Drug (hereafter "PR") in view of Erle et al. Acta Diabetol (1999) 36:61-65 (hereafter "Erle et al."). Applicant respectfully traverses this rejection.

According to the rejection, PR discloses a method of using metformin and glyburide as initial therapy for patients with type 2 diabetes. Erle et al. disclose that it is known to use low-dose glyburide plus metformin. Therefore, it would be obvious to use the low dose glyburide of Erle et al. in the method of PR.

First, as is clear in the application and as noted above in the discussion of the rejection of claims 5 and 19 and claims 7 and 20 under 35 U.S.C. §112, a "low dose" formulation in the instant claims can refer to a low dose of metformin, a low dose of glyburide, or a low dose of both. Erle et al. clearly refers *only* to a low dose of glyburide. (Note that the lowest dose of metformin given in Erle et al. is 800 mg.) Consequently, on its face, Erle et al. cannot possibly relate to claims 38, 40-

41, 44, 48-54, 56-60 and 67 of the instant application. Moreover, there is nothing in Erle et al. or PR to suggest the bioavailability or particle size requirements of claims 61-66.

Next, the very lowest dose of glyburide given in Erle et al. is 5 mg. In the instant application, the starting daily dosage of glyburide can be as low as 0.5 mg to 3.5 mg before the amount is titrated up. See the instant specification on, for example, page 9. Nowhere is this kind of dosing contemplated in Erle et al.

PR does not suggest any dosing at all. Therefore, the combination of Erle et al. and PR does not make obvious applicant's invention.

For these reasons, applicant requests that this rejection be withdrawn.

Claims 1-36 were also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-76 of copending application no. 09/432,465. While applicant disagrees, applicant intends to file a terminal disclaimer, if necessary, when the application(s) are otherwise in condition for allowance.

Finally, claims 1-36 were provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 47-66 of copending application no. 09/432,465. Again, while applicant disagrees, applicant intends to cancel claims 47-66, without prejudice, in copending application no. 09/432,465.

In view of the foregoing, reconsideration of this application, withdrawal of the rejections, consideration of the supplemental information disclosure statement, approval of the formal drawings submitted on April 18, 2001, and allowance of all the pending claims are all respectfully requested.

Respectfully submitted,

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